RPPPGRRPFFHPVGEADYFEYHQEG (SEQ ID NO:22), PDVPPGAI (SEQ ID NO:23), PGAIEQGPA (SEQ ID NO:24), GPSTGPRG (SEQ ID NO:25), GQGDGGRRK (SEQ ID NO:26), DGGRRKKGGWFGKHR (SEQ ID NO:27), GKHRGQGGSN (SEQ ID NO:28), GQGGSNPK (SEQ ID NO:29), NPKFENIA (SEQ ID NO:30), RSHVERTT (SEQ ID NO:31), VFVYGGSKT (SEQ ID NO:32), GSKTSLYNL (SEQ ID NO:33), GMAPGPGP (SEQ ID NO:34), PQPGPLRE (SEQ ID NO:35), CNIRVTVC (SEQ ID NO:36), RVTVCSFDDG (SEQ ID NO:37), PPWFPPMVEG (SEQ ID NO:38).

22. (twice amended) The method of claim 19 wherein the individual is tested for the presence of antibodies to GAGAGAGAGAGAGAGAGAGAGA (SEQ ID NO:7).

Remarks

The application has been amended to identify each amino acid sequence with the appropriate Sequence Identification Number and to provide paper and computer readable copies of the "Sequence Listing" in order to comply with the requirements of 37 C.F.R. 1.821 through 1.825.

Additionally, in the chart on page 19, line 25, the single letter codes for phenylalanine, asparagine and tryptophan have been added because these amino acids are used in SEQ ID NOS:12, 21, 26-29, 32 and 35-37 and this row of abbreviations was inadvertently left out.

Two tables were inadvertently labelled as Table 5. The second Table 5 has been renumbered to Table 6. Table 6 has been amended to add the Sequence Identification Numbers and decrease the width of the table to less than five inches to comply with 37 CFR 1.58(c). In claim 15, line 43, a typographical error has been corrected from "gcardiomyopathy" to "cardiomyopathy", which agrees with the spelling on page 17, line 32.

On page 30, line 8, the sequence "PPPGMRRP" has been revised to correct a typographical error. The seventh base should be a "P", as evidenced by the sequence to which it is referring in line 7, "PPPGMRPP".

On page 30, line 28, the sequence "PPPGRMPP" has two bases transposed. The sequence has been revised to match the sequence to which it is referring in the protocol in the above paragraph and on lines 24 and 29, "PPPGMRPP".

On page 43, line 18, the reverse primer was inadvertently listed as being the same sequence as the forward primer. Page 43, line 1, states that the method of the invention is partially based on the assay of the cited reference, Saito, et al., J. Exp. Med. 169:2192 (1989). The reverse primer of the invention has been corrected to reflect the reverse primer disclosed in the reference, which is attached for the examiner's review.

On page 46, line 16, an additional repeat was added to the eleven repeat sequence "GAGAGAGAGAGAGAGAGAGAGA", because the twelfth repeat was inadvertently deleted

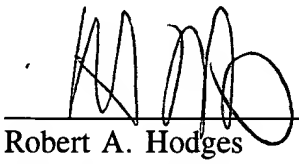
from the application. Support for this amendment is found at page 11, line 11, page 25, lines 26 and 29, and claims 8, 9, 19 and 20, wherein each occurrence of the glycine-alanine repeat sequence recites 12 repeats.

Declaration under 37 CFR 1.821(f)

I declare that the material on the diskette is identical to the enclosed paper copy of the "Sequence Listing" and the sequences as filed in the application on January 13, 1997 as required by 37 CFR 1.821(f), include no new matter to the application as required by 37 CFR 1.821(g), are encoded in a subset of ASCII as required by 37 CFR 1.825(b) and are contained within one file on a single diskette as required by 37 CFR 1.825(d). All statements are made on information and belief are believed to be true and I further declare that these statements were

made with the knowledge that willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,



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Date: October 22, 1997

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APPENDIX

We claim:

1. A vaccine for alleviating or preventing autoimmune disorders induced by infection with Epstein-Barr virus comprising

Epstein-Barr virus or a component thereof in a pharmaceutically acceptable carrier for administration of the virus or viral component in an amount and mode of administration effective to alleviate or prevent the autoimmune disorders.

2. The vaccine of claim 1 wherein one or more structures of the Epstein-Barr virus are removed or altered to decrease the potential that the vaccine will induce an autoimmune disorder.

3. The vaccine of claim 1 wherein the component of Epstein-Barr virus is selected from the group consisting of peptides or proteins expressed from recombinant DNA or RNA with sequence identity to Epstein-Barr virus, viral DNA or RNA, and carbohydrate components of the Epstein-Barr virus.

4. The vaccine of claim 1 wherein the Epstein-Barr virus comprises the nuclear antigen 1 protein not including a peptide sequence selected from the group consisting of PPPGRRP, GRGRGRGG and RGRGREK.

5. The vaccine of claim 1 in a pharmaceutical carrier for administration by injection.

6. A diagnostic test comprising

reagents which can be used to detect levels of antibodies to Epstein-Barr virus, indicators of Epstein-Barr infection of cells, or levels of Epstein-Barr DNA or protein in a patient, and

control samples from individuals not at risk of developing an autoimmune disease, and

means for determining the differences in levels of a patient and control samples to distinguish individuals at higher risk of developing an autoimmune disease from those at lower risk of developing an autoimmune disease.

7. The diagnostic test of claim 6 wherein the reagents are used in assays based upon the relative presence of an antibody, cellular proliferation, molecular binding, cytokine production, skin reaction, or cell surface antigen.

8. (amended) The diagnostic test of claim 6 wherein the reagents are used to detect antibodies to peptides from Epstein-Barr virus selected from the group consisting of PPPGRRP (SEQ ID NO:1), GRGRGRGG (SEQ ID NO:2), RGRGREK (SEQ ID NO:3), GAGAGAGAGAGAGAGAGAGAGAGA (SEQ ID NO:7), GPQRRGGDNHGRGRGRGRGRGGGRPG (SEQ ID NO:13),

GGSGSGPRHRDGVRRPQKRP (SEQ ID NO:14), RPQKRPSC (SEQ ID NO:15), QKRPSCIGCKGTHGGTG (SEQ ID NO:16), GTGAGAGARGRGG (SEQ ID NO:17), SGGRGRGG (SEQ ID NO:18), RGGSGGRRGRGR (SEQ ID NO:19), RARGRGRGRGEKRPRS (SEQ ID NO:20), SSSSGSPPRRPPPGR (SEQ ID NO:21), RPPPGRRPFFHPVGEADYFEYHQEG (SEQ ID NO:22), PDVPPGAI (SEQ ID NO:23), PGAIEQGPA (SEQ ID NO:24), GPSTGPRG (SEQ ID NO:25), GQGDGGRRK (SEQ ID NO:26), DGGRRKKGGWFGKHR (SEQ ID NO:27), GKHRGQGGSN (SEQ ID NO:28), GQGGSNPK (SEQ ID NO:29), NPKFENIA (SEQ ID NO:30), RSHVERTT (SEQ ID NO:31), VFVYGGSKT (SEQ ID NO:32), GSKTSLYNL (SEQ ID NO:33), GMAPGPGP (SEQ ID NO:34), PQPGPLRE (SEQ ID NO:35), CNIRVTVC (SEQ ID NO:36), RVTVCSFDDG (SEQ ID NO:37), PPWFPPMVEG (SEQ ID NO:38).

9. (amended) The diagnostic test of claim 8 comprising reagents for detection of antibodies to GAGAGAGAGAGAGAGAGAGAGA (SEQ ID NO:7).

10. The diagnostic test of claim 6 for testing patients identified with or at risk of developing systemic lupus erythematosus comprising control samples from individuals with systemic lupus erythematosus.

11. A method for preventing or alleviating autoimmune disorders induced by infection with Epstein-Barr virus comprising

vaccinating or administering to a individual at risk of developing, or who has been identified as having symptoms associated with, an autoimmune disorder induced by infection with Epstein-Barr virus,

Epstein-Barr virus or a component thereof in a pharmaceutically acceptable carrier for administration of the virus or viral component in an amount and mode of administration effective to alleviate or prevent the autoimmune disorders.

12. The method of claim 11 wherein one or more structures of the Epstein-Barr virus are removed or altered to decrease the potential that the vaccine will induce an autoimmune disorder.

13. The method of claim 11 wherein the component of Epstein-Barr virus is selected from the group consisting of peptides or proteins expressed from recombinant DNA or RNA with sequence identity to Epstein-Barr virus, viral DNA or RNA, and carbohydrate components of the Epstein-Barr virus.

14. (amended) The method of claim 11 wherein the Epstein-Barr virus comprises the nuclear antigen 1 protein not including a peptide sequence selected from the group consisting of PPPGRRP (SEQ ID NO:1), GRGRGRGG (SEQ ID NO:2) and RGRGREK (SEQ ID NO:3).

15. (amended) The method of claim 11 wherein the individual has symptoms of or is at risk of developing an autoimmune disorder selected from the group consisting of systemic lupus erythematosus, Sjogren's syndrome, rheumatoid arthritis, juvenile onset diabetes mellitus, Wegener's granulomatosis, inflammatory bowel disease, polymyositis, dermatomyositis, multiple endocrine failure, Schmidt's syndrome, autoimmune uveitis, Addison's disease, adrenalitis, primary biliary cirrhosis, Graves' disease, thyroiditis, Hashimoto's thyroiditis, autoimmune thyroid disease, pernicious anemia, lupoid hepatitis, demyelating diseases, multiple sclerosis, subacute cutaneous lupus erythematosus, hypoparathyroidism, Dressler's syndrome, myasthenia gravis, autoimmune thrombocytopenia, idiopathic thrombocytopenic purpura, hemolytic anemia, autoimmune hemolytic anemia, pemphigus vulgaris, pemphigus, bullous pemphigoid, dermatitis herpetiformis, alopecia areata, autoimmune cystitis, pemphigoid, scleroderma, progressive systemic sclerosis, CREST syndrome (calcinosis, Raynaud's esophageal dysmotility, sclerodactyly, and telangiectasia), adult onset diabetes mellitus (Type II diabetes), male or female autoimmune infertility, ankylosing spondylitis, ulcerative colitis, Crohn's disease, mixed connective tissue disease, polyarteritis nodosa, systemic necrotizing vasculitis, juvenile onset rheumatoid arthritis, glomerulonephritis, atopic dermatitis, atopic rhinitis, Goodpasture's syndrome, Chagas' disease, sarcoidosis, rheumatic fever, asthma, recurrent abortion, anti-phospholipid syndrome, farmer's lung, erythema multiforme, postcardotomy syndrome, Cushing's syndrome, autoimmune chronic active hepatitis, bird-fancier's lung, allergic encephalomyelitis, toxic necrodermal lysis, alopecia, Alport's syndrome, alveolitis, allergic alveolitis, fibrosing alveolitis, interstitial lung disease, erythema nodosum, pyoderma gangrenosum, transfusion reaction, chronic fatigue syndrome, fibromyalgia, Takayasu's arteritis, Kawasaki's disease, polymyalgia rheumatica, temporal arteritis, giant cell arteritis, Sampter's syndrome (triaditis also called, nasal polyps, eosinophilia, and asthma), Behcet's disease, Caplan's syndrome, dengue, encephalomyositis, endocarditis, myocarditis, endomyocardial fibrosis, endophthalmitis, erythema elevatum et diutinum, psoriasis, erythroblastosis fetalis, fascitis with eosinophilia, Shulman's syndrome, Felty's syndrome, filariasis, cyclitis, chronic cyclitis, heterochromic cyclitis, Fuch's cyclitis, IgA nephropathy, Henoch-Schonlein purpura, glomerulonephritis, cardiomyopathy, post vaccination syndromes, Hodgkin's and non-Hodgkin's lymphoma, renal cell carcinoma, Eaton-Lambert syndrome, relapsing polychondritis.

16. (amended) The method of claim 11 wherein the vaccine is administered prior to infection with Epstein-Barr virus.

17. (amended) The method of claim 11 wherein the vaccine is administered to an individual who has or has previously had an infection with Epstein-Barr virus.

18. (amended) The method of claim 11 wherein the autoimmune disorder is systemic lupus erythematosus.

19. (amended) A method for determining the likelihood that an individual has an autoimmune disorder induced by Epstein-Barr virus, or is at risk for developing such an autoimmune disorder, comprising

obtaining a sample from the individual to be tested,

mixing the sample with reagents which can be used to detect levels of antibodies to Epstein-Barr virus, indicators of Epstein-Barr infection of cells, or levels of Epstein-Barr DNA or protein in a patient,

analyzing the sample, and

comparing the analysis of the sample with results obtained with control samples from individuals not at risk of developing an autoimmune disease to determine if the differences in levels of the individual and control samples indicates the individual is at a higher risk of developing an autoimmune disease than controls who are at lower risk of developing an autoimmune disease.

20. (amended) The method of claim 19 wherein the reagents are used in assays based upon the relative presence of an antibody, cellular proliferation, molecular binding, cytokine production, skin reaction, or cell surface antigen.

21. (twice amended) The method of claim 19 wherein the reagents are used to detect antibodies to peptides from Epstein-Barr virus selected from the group consisting of PPPGRRP (SEQ ID NO:1), GRGRGRGG (SEQ ID NO:2), RGRGREK (SEQ ID NO:3), GAGAGAGAGAGAGAGAGAGAGAGA (SEQ ID NO:7), GPQRRGGDNHGRGRGRGRGRGGGRPG (SEQ ID NO:13), GGSGSGPRHRDGVRRPQKRP (SEQ ID NO:14), RPQKRPSC (SEQ ID NO:15), QKRPSCIGCKGTHGGTG (SEQ ID NO:16), GTGAGAGARGRGG (SEQ ID NO:17), SGGRGRGG (SEQ ID NO:18), RGGSGGRRGRGR (SEQ ID NO:19), RARGRGRGRGEKRPRS (SEQ ID NO:20), SSSSGSPPRRPPPGR (SEQ ID NO:21), RPPPGRRPFFHPVGEADYFEYHQEG (SEQ ID NO:22), PDVPPGAI (SEQ ID NO:23), PGAIEQGPA (SEQ ID NO:24), GPSTGPRG (SEQ ID NO:25), GQGDGGRRK (SEQ ID NO:26), DGGRRKKGGWFGKHR (SEQ ID NO:27), GKHRGQGGSN (SEQ ID NO:28), GQGGSNPK (SEQ ID NO:29), NPKFENIA (SEQ ID NO:30), RSHVERTT (SEQ ID NO:31), VFVYGGSKT (SEQ ID NO:32), GSKTSLYNL (SEQ ID NO:33), GMAPGPGP (SEQ ID NO:34), PQPGPLRE (SEQ ID NO:35), CNIRVTVC (SEQ ID NO:36), RVTVCSFDDG (SEQ ID NO:37), PPWFPPMVEG (SEQ ID NO:38).

22. (twice amended) The method of claim 19 wherein the individual is tested for the presence of antibodies to GAGAGAGAGAGAGAGAGAGAGAGA (SEQ ID NO:7).

23. (amended) A method for screening of therapeutics for prevention or alleviation of autoimmune disorders induced by infection with Epstein-Barr virus comprising

administering the therapeutic to be tested to an animal vaccinated with Epstein-Barr virus or a component thereof in an amount and mode of administration effective to induce an autoimmune response.

24. (amended) The method of claim 23 further comprising administering the therapeutic to an animal which does not develop an autoimmune response when vaccinated with the same composition effective in another strain of the animal, and determining the difference in response to the therapeutic.

25. (amended) The method of claim 24 wherein the animals are mice.

26. (amended) A method for screening for genetic markers or risk factors for development of autoimmune disorders induced by infection with Epstein-Barr virus comprising comparing the responses of different strains of the same species of an animal vaccinated with Epstein-Barr virus or a component thereof in an amount and mode of administration effective to induce an autoimmune response in at least one of the strains and comparing the differences in the genetics of the different strains to identify potential genetic markers or risk factors.